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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

In re application of:

Applicants	DeBenedetti, Arrigo, *et al.*	:	Docket No:	101611/507550
Serial No.	09/916,017	:	Group Art Unit:	1635
Filed:	July 26, 2001	:	Examiner:	J. Angell

For: CANCER GENE THERAPY BASED ON TRANSLATIONAL CONTROL OF A SUICIDE GENE

DECLARATION UNDER 37 CFR 1.132

Box Amendment Fee
The Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This declaration under 37 CFR Sec. 1.132 is supportive of the Amendment and Response filed herewith. I, Arrigo DeBenedetti, declare and say:

1. That I am a citizen of Italy, US permanent resident and that I am one of the co-inventors in the above-referenced patent application; that I have been employed by Louisiana State University Health Sciences Center-Shreveport since 1992, that I have been Associate Professor in the Biochemistry Department since 1998, and I was and still am, engaged in a research program in the field of cancer treatment and particularly genetic therapeutics;

2. That I am familiar with the above-identified patent application Ser. No. 09/916,017, that I have reviewed the January 22, 2003, Office Action in the above captioned case, and that I am familiar with the following references cited by the Examiner: Shimogori *et al.* (BBRC Vol. 223:544-548; 1996); van der Velden et al. 1999, cite in IDS, Table 1, p. 90 Koromilas *et al.* (EMBO 1992, cited in IDS) in view of Li B.D. *et al.* (Cancer 1997, cited in IDS) and further in view of Anderson L.M. *et al.* (Gene Therapy 1999, cited in IDS).

3. That I have analyzed the sequence described in Shimogori et al., using a computer program called M-fold, which analyzes possible structures in RNA using Zucker's minimal energy calculations. That the only stem of possible stability is the 47 nt oligonucleotide marked as hatched boxes in the model on page 820 of the paper listed as "cgggguuuggcgggggcgcuccaugggucaggccagccgggccaccc." That this particular structure is destabilized by some bulges and G-U base pairs. That upon calculation of stability, the 5'UTR described by Shimogori would provide a secondary structure conformation having a stability ΔG of about -22 Kcal/Mol. In addition, that the construct described is only about 56% G/C-rich.

4. That the particular region of ODC described in Shimogori *et al.* is insufficient to confer regulation by the level of eIF4E as shown by Shantz LM, Pegg AE. (Int J Biochem Cell Biol. 1999, 31(1):107-22. Review). That the construct described by Shigomori would not work in intact cells but only in cell-free systems like reticulocyte lysate after *in vitro* transcription. That such sequence does not provide the appropriate level of stability ($\Delta G \geq$ about 50 Kcal/Mol) to selectively regulate translation of the open reading frame.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Further declarant sayeth not.

Arrigo DeBenedetti

5-8-03
Date